REMARKS

I. Claim Status

As set forth in the Office Action Summary, Claims 1-4, 6-8, 10-13, 15-16, 18-49 and 52-59 are pending. Claims 25-45 stand withdrawn. Claims 21, 49 and 57-59 are canceled herein. Claims 20 is amended. Applicants reserve the right to file at least one continuation and/or divisional application directed to any canceled subject matter.

Entry of the foregoing amendments of the above-identified application are respectfully requested.

II. Claim Rejections Under 35 U.S.C. § 112

Claims 1-3, 6-8, 10-13, 15-16, 18-24, 46-49 and 52-59 were rejected under 35 U.S.C. § 112, first paragraph as purportedly lacking enablement.

The Office acknowledged that the specification enables a method of promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis (MS) subject. However, the Examiner indicated that a person of ordinary skill in the art would not have predicted that anti-VLA-4 antibodies would be useful for treating other clinical disorders involving demyelination.

Attached as Exhibit A are test results supporting the argument that anti-VLA-4 antibodies are useful in the treatment of other clinical disorders involving demyelination. Guinea pigs were treated every other day with natalizumab for either 28 days or 56 days during the chronic phase of demyelination. Applicants submit that one of skill in the art could note the improvement in reduction of demyelination between the 28 day treatment and 56 day treatment and determine that treatment with natalizumab in a more chronic fashion (*i.e.*, administered for 6 months or more) would produce even further reduction of demyelination.

In this study, chronic demyelination was induced in guinea pigs. Natalizumab was administered and thoracic sections were taken from the guinea pigs during short and long term treatments. Sections were visualized with Weil Myelin stain to reveal areas of demyelination indicated by the absence of blue stain. The score for the

entire spinal cord, after 28 days of treatment with natalizumab, was significantly improved compared to its vehicle match. Extensive demyelination was seen throughout the entire perimeter of the cord extending inwards to the parenchyma at 56 days post treatment with only vehicle (control). In contrast, considerable reduction in demyelinated lesions were seen after 56 days of natalizumab treatment.

Applicants would be pleased to provide the data in the form of a Declaration Under 37 C.F.R. § 1.132 if the Examiner deems it useful. This data illustrates that natalizumab is effective in reducing demyelination and treating demyelinating diseases, as well as promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis subject.

Applicants request that this rejection be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-58 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-56 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,840,299. Claims 1-4, 19-21, 49, 57 and 58 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247 in view of U.S. Patent No. 6,284,473. Claims 1-4, 19-20, 22-23, 49, 57 and 59 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/15247 or U.S. Patent No. 5,840,299, each in view of U.S. Patent No. 6,753,135. Claims 1-4, 19-21, 57 and 58 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,840,299 in view of U.S. Patent No. 6,602,885.

Specifically, the Office states that the primary references, the '247 publication and the '299 patent, teach treatment of multiple myeloma (MM) and MS, respectively, using anti-VLA-4 antibodies. The Office acknowledges that these publications do not explicitly teach the remyelination of nerve cells or the reversal of paralysis. However, the Office argues that because the treatment methods are the same, the referenced methods inherently result in remyelination of nerve cells and reversing paralysis. The Office also acknowledges that the publications do not explicitly teach chronic administration weekly or monthly over a period of at least six months or a year.

Applicants submit that the chronic administration of natalizumab has displayed unexpected benefits in the treatment of demyelinating conditions. As shown in the attached data at Exhibit A, the administration of natalizumab over time caused reduction in demyelination. In the study, guinea pigs were given natalizumab during short and long term treatments. Extensive demyelination was seen throughout the entire perimeter of the cord extending inwards to the parenchyma at 56 days post treatment with only vehicle (control). In contrast, considerable reduction in demyelinated lesions was seen after 28 days, and further reduction was seen after 56 days of natalizumab treatment. As noted above, Applicants would be pleased to provide this data in the form of a Declaration Under 37 C.F.R. § 1.132 if the Office wishes.

None of the cited references disclose these benefits of chronic administration. Thus, not only do the cited references fail to disclose chronic administration of anti-VLA-4 antibodies, but the references fail to disclose the reduction of demyelination caused by demyelinating disease states. Accordingly, at the time invention was made one of ordinary skill in the art would not have had an expectation of success in achieving the effect of reduction of demyelination, and accordingly would not have combined the elements of the cited references to arrive at the present invention. Further, there is no motivation to combine the secondary references cited by the Office with WO 0015247 and U.S. Patent No. 5,840,299. Even if combined, the combination fails to resolve the differences between the primary references, the '299 patent and the '247 publication, and the claims in issue.

In light of the above, Applicants request that these rejections be withdrawn.

CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this paper, or the application in general, the Examiner is respectfully urged to telephone Applicants' undersigned representative so that prosecution of this application may be expedited.

Respectfully submitted,

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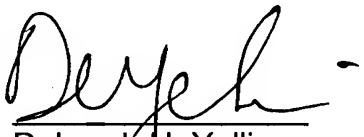
Date: June 21, 2007 By: 

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